

## **REMARKS**

The July 6, 201 Official Action and the references cited therein have been carefully considered. In view of the amendments submitted herewith and these remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, it is noted that a shortened statutory response period of three (3) months was set in the Official Action. The initial due date for response, therefore, was October 6, 2011. This response is being filed within the three month statutory period. Claims 22, 26, 27, 32, 36, 38, 39, 41, 42, and 55 stand finally rejected.

As another preliminary matter, Applicants have amended claims 27 and 39 in keeping with the Examiner's helpful suggestion, thereby rendering the objection to these claims moot.

Claims 22, 26, 27, 32, 36, 38, 39, 41, 42, and 55 are newly rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Claim 22 has been amended to reinsert the term "contacting", thereby removing this ground of rejection.

The Examiner has maintained the rejection of claims 22, 26, 32, 36, 38, 39, and 55 under 35 USC §103(a) as allegedly unpatentable over US Patent 5,994,084 to Anderton, in view of Singh1 Singh2, Graves, US Patent 6,593,512 to Vitek and Litersky.

Claims 22, 26, 27, 32, 36, 38, 39, and 55 remain rejected under 35 USC §103(a) as allegedly unpatentable over the '084 patent to Anderton in view of Lau et al., Graves, Vitek, Hasegawa and Yamamoto.

At page 20 of the Official Action, the Examiner has maintained the rejection of claim 27 as allegedly obvious over the '084 patent to Anderton, Singh1, Singh2, Graves, Vitek and Litersky and further in view of Hasegawa.

Claims 41 and 42 also remain rejected as allegedly obvious over the combination of US Patent 5,994,084 to Anderton, in view of Singh1 Singh2, Graves, US Patent 6,593,512 to Vitek and Litersky or US Patent 5,994,084 to Anderton, Lau, Graves, US Patent 6,593,512 to Vitek Hasegawa, Yamamoto and further in view of Zhu.

The Examiner has also maintained the rejection of claim 22, 26, 32, 36, 38, 39, 41, 42 and 55 based on obviousness double patenting

The foregoing objections and rejections constitute all of the grounds set forth in the July

6, 2011 Official Action for refusing the present application. For the reasons given below, each of these grounds of rejection are respectfully traversed.

**THE CLAIMS AS AMENDED ARE PATENTABLE OVER  
THE ART RELIED ON BY THE EXAMINER**

Applicants again express their frustration that the Examiner has once again rejected the claims based on obviousness citing prior art that fails to place the methods presently claimed in the public domain. The Examiner is once again reminded that “silence in a reference is not a proper substitute for adequate disclosure of facts from which a conclusion of obviousness may justifiably follow”. In re Burt, 148 U.S.P.Q. 548 (CCPA 1966). Applicants reiterate that with respect to all of the prior art rejections and obviousness-type double patenting rejections, many of the predetermined sites on tau phosphorylated by CKI in the pending claims were unknown prior to the present invention as was their association with pathological forms of tau. Notably the claims has been amended to require detection of these novel sites phosphorylated by CK1, rather than all and any phosphorylation sites on tau that may or may not be associated with disease.

At the beginning of page 8 of the action, the Examiner responds to our previous argument that the invention as claimed requires to the use of a single kinase (CK1), by stating “the claims do not exclude contacting with an additional kinase polypeptide, e.g. CaM kinase II, particularly in light of the specification, which discloses, “ the present application also discloses that a combination of kinases is required to phosphorylate the majority of the phosphorylation sites disclosed herein...(paragraph bridging pp 14-15).”

In response, it should first be noted that the claim is concerning with identifying candidate substances which inhibit the phosphorylation of a tau protein by casein kinase (CK1). If a further kinase was used in addition to CK1, it would not be possible to carry out the method as claimed as one would not be able to determine which kinase the candidate substance actually inhibited. Accordingly, Applicants submit that the interpretation by the Examiner confounds the objective of the method stated in the preamble of the claim. Moreover, the Examiner is already on record stating that the use of a combination of kinases constitutes a separate and distinct invention. A similar argument is used by the examiner in the last paragraph of page 10 in which he again states that “by determining whether a candidate substance inhibits

CaM kinase II phosphorylation of S416 of tau in the presence of a combination of CaM kinases II and CK1, one would have practiced the claimed method”. With respect to claim 12, the examiner states “There is no claim limitation that excludes a combination of kinases in the claims”. Applicants reiterate all of the arguments set forth in the previous response. To summarize, the prior art relied on by the Examiner fails to place the invention in the hands of the public. The disclosures, when considered in combination, amount to mere speculation and an invitation to experiment to arrive at, and unambiguously identify those CK1 phosphorylated sites on tau which are associated with Alzheimer’s pathology. As such, the Examiner has clearly failed to establish a prima facie case of obviousness.

In order to expedite an issuance of a notice of allowance in this application, claims 22 and 36 have been amended to recite “consisting of” language. This amendment precludes the Examiner’s erroneous interpretation of the claims and should place the case in condition for allowance. The aforementioned amendments are fully supported by the specification as filed and do not introduce features requiring new consideration and search and consideration. Claim 36 has been amended such that is now in independent form and incorporates all of the features of claim 22 from which it previously depended. This amendment was necessitated by the Examiner’s insistence that the claims read on the use of a combination of kinases, which is clearly in error given that this interpretation confounds the objective of the claim to identify CK1 phosphorylated sites and moreover, this subject matter is considered a separate and patentably distinct invention. Finally, the Examiner’s attention is drawn to dependent claims 32 and 55 which recite previously unidentified novel CK1 phosphorylation sites on tau associated with Alzheimer’s dementia.

In view of the aforementioned amendments, Applicants submits that the §103 rejection of claims 22, 26, 27, 32, 36, 38, 39, 41, 42, and 55 based on the various references cited by the Examiner is untenable and should be withdrawn upon reconsideration.

**THE OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTIONS OF THE AMENDED CLAIMS ARE WITHOUT MERIT AND SHOULD BE WITHDRAWN**

The impropriety of the present rejection has been addressed at length in applicant’s previous response. Applicants reiterate the Examiner’s broad interpretation of claim 22 is

completely inappropriate given the amendments presented herein. First, the claims can no longer be interpreted to read on the use of a combination of kinases nor do they read on “necessarily analyzing any and all sites of phosphorylation of tau”. Applicants take exception to the Examiner’s interpretation of ‘084 to Anderton regarding the use of any and all kinases. How can Anderton be stated to contemplate the use of CK1 when as the Examiner acknowledges it was not known (at the time Anderton was filed) that CK1 phosphorylates tau. The Examiner relies on Singh for this disclosure. However, Singh was using a combination of kinases so the skilled person is left to wonder which of the kinases were actually responsible for the phosphorylation event. Additionally, the claims of ‘084 patent are drawn to unique and distinct kinases which are not related to CK1. Inasmuch as the use of a combination of kinase enzymes is precluded by the present amendments to the claim, Applicants submit that the presently claimed method cannot be considered an obvious variation of the invention claimed in the ‘084 patent. It is clear that the disclosure in the ‘084 patent when combined with Singh fails to place the method of claims 22 and 36 as amended in the public domain and nor would the skilled person having the ‘084 disclosure before him or her in combination with Singh arrive at the subject matter instantly claimed. In view of these clear differences between the present claims as amended and claim 6 in the ‘084 patent in view of Singh, the grant of a patent on the present application can not conceivably result in a time-wise extension of the ‘084 patent grant. Thus the rejections on this ground should be withdrawn.

At page 28 of the Official Action, the Examiner has maintained the obviousness double patenting rejection of claims 41 and 42 based on claim 6 in the ‘084 patent to Anderton in view of Singh3, Graves, Vitek, Hasegawa, and Yamamoto. As above, this combination of references does not place the invention currently claimed in the hands of the public. The CK1 phosphorylation sites in tau associated with Alzheimer’s pathology were not unambiguously determined until the present invention. As such the granting of claims 41 and 42 cannot be construed as an impermissible extension of the ‘084 patent term. Accordingly, the rejection should be withdrawn upon reconsideration.

## **CONCLUSION**

It is respectfully requested that the amendments presented herewith be entered in this application, since the amendments are primarily formal, rather than substantive in nature. This

amendment is believed to clearly place the pending claims in condition for allowance. The claims as presently amended are also believed to eliminate certain issues and better define other issues which would be raised on appeal, should an appeal be necessary in this case.

In view of the amendments and remarks presented herein, it is respectfully urged that the rejections set forth in the July 6, 2011 Official Action be withdrawn and that this application be passed to issue. In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,

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